(FILE 'HOME' ENTERED AT 15:35:19 ON 20 JUN 2001)

FILE 'MEDLINE, EMBASE, SCISEARCH, CAPLUS, USPATFULL' ENTERED AT 15:35:47 ON 20 JUN 2001

L1 2996 S (ANTIBOD? OR IMMUNOGLOBULIN?) (3P) LIPASE?
L2 113380 S (ANTIBOD? OR IMMUNOGLOBULIN?) (3P) (MUCOS? OR INTAKE OR ORAL?
L3 604 S L1 AND L2
L4 789 S (ANTIBOD? OR IMMUNOGLOBULIN?) (5A) LIPASE?
L5 101316 S (ANTIBOD? OR IMMUNOGLOBULIN?) (P) (MUCOS? OR INTAKE OR ORAL? digest? or fed? or food? or gastro? or gastri?
L6 62 S L4 AND L5
L7 43 DUP REM L6 (19 DUPLICATES REMOVED)
L8 14537 S (ANTIBOD? OR IMMUNOGLOBULIN?) (3A) (MUCOS? OR INTAKE OR ORAL?
L9 37 S L8 AND L4
L10 31 DUP REM L9 (6 DUPLICATES REMOVED)
L11 1009 S L1 AND (WEIGHT? OR DIET? OR (FAT METABOLI?))
L12 58 S L1 AND L8
L13 50 DUP REM L12 (8 DUPLICATES REMOVED)
L14 35 S L11 AND L8
L15 35 DUP REM L14 (0 DUPLICATES REMOVED)

L10 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:64709 CAPLUS
DOCUMENT NUMBER: 130:138298
TITLE: Decreased fat absorption with an anti-**lipase antibody**
INVENTOR(S): Pimentel, Julio L.
PATENT ASSIGNEE(S): Ximed Group Plc, UK
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902187	A1	19990121	WO 1998-GB1998	19980706
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882326	A1	19990208	AU 1998-82326	19980706
EP 1001809	A1	20000524	EP 1998-932392	19980706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
BR 9815504	A	20001128	BR 1998-15504	19980706
NO 2000000052	A	20000302	NO 2000-52	20000106

PRIORITY APPLN. INFO.:
US 1997-888202 A 19970707
US 1997-882202 A 19970707
WO 1998-GB1998 W 19980706

AB A method for the decrease of fat absorption in any animal, wherein the animal is fed an **antibody** produced against **lipase**, an enzyme which is required for fat absorption. Avian egg-derived anti-**lipase antibodies** are disclosed for treating obesity in a mammal or an avian. Also, avian egg-derived **antibodies** (IgYs) against **gastrointestinal** enzyme such as amylase, trypsin, chymotrypsin, protease and other enzyme or antigen are used for reducing absorption of nutrients such as proteins, carbohydrates and lipids. These **antibodies** are mixed in **food** (concd., additive-added, refrigerated or frozen food) for human or animal consumption.

TI Decreased fat absorption with an anti-**lipase antibody**
AB A method for the decrease of fat absorption in any animal, wherein the animal is fed an **antibody** produced against **lipase**, an enzyme which is required for fat absorption. Avian egg-derived anti-**lipase antibodies** are disclosed for treating obesity in a mammal or an avian. Also, avian egg-derived **antibodies** (IgYs) against **gastrointestinal** enzyme such as amylase, trypsin, chymotrypsin, protease and other enzyme or antigen are used for reducing absorption of nutrients such as proteins, carbohydrates and lipids. These **antibodies** are mixed in **food** (concd., additive-added, refrigerated or frozen food) for human or animal consumption.

IT Fats and Glyceridic oils, biological studies

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(absorption; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Bird (Aves)
Chicken (Gallus domesticus)
Digestive system mucosa
Duck
Egg (animal)
Egg yolk
Encapsulation
Feed additives
Food
Freeze drying
Frozen foods
Goose
Liposomes (drug delivery systems)
Liquids
Mammal (Mammalia)
Mold (fungus)
Nutrients
Obesity
Oral drug delivery systems
Pheasant
Pigeon
Powders
Primate
Quail
Ruminant
Spray drying
Turkey
Yeast
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT **Antibodies**
IgY
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Carbohydrates, biological studies
Lipids, biological studies
Proteins (general), biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Antigens
Monoclonal **antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(fat-hydrolytic; avian egg-derived anti-**lipase** or anti-

gastrointestinal enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Concentration (process)
Refrigeration
(food; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Enzymes, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(gastrointestinal; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Animal cell line
Bacteria (Eubacteria)
Plant (Embryophyta)
(lipase; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Mammal (Mammalia)
(monogastric; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT 9000-92-4, Amylase 9001-62-1, Lipase 9001-92-7, Protease 9002-07-7, Trypsin 9004-07-3, Chymotrypsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

L10 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:64709 CAPLUS
DOCUMENT NUMBER: 130:138298
TITLE: Decreased fat absorption with an anti-**lipase antibody**
INVENTOR(S): Pimentel, Julio L.
PATENT ASSIGNEE(S): Ximed Group Plc, UK
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902187	A1	19990121	WO 1998-GB1998	19980706
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882326	A1	19990208	AU 1998-82326	19980706
EP 1001809	A1	20000524	EP 1998-932392	19980706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
BR 9815504	A	20001128	BR 1998-15504	19980706
NO 2000000052	A	20000302	NO 2000-52	20000106

PRIORITY APPLN. INFO.:
US 1997-888202 A 19970707
US 1997-882202 A 19970707
WO 1998-GB1998 W 19980706

AB A method for the decrease of fat absorption in any animal, wherein the animal is fed an **antibody** produced against **lipase**, an enzyme which is required for fat absorption. Avian egg-derived anti-**lipase antibodies** are disclosed for treating obesity in a mammal or an avian. Also, avian egg-derived **antibodies** (IgYs) against **gastrointestinal** enzyme such as amylase, trypsin, chymotrypsin, protease and other enzyme or antigen are used for reducing absorption of nutrients such as proteins, carbohydrates and lipids. These **antibodies** are mixed in **food** (concd., additive-added, refrigerated or frozen food) for human or animal consumption.

TI Decreased fat absorption with an anti-**lipase antibody**
AB A method for the decrease of fat absorption in any animal, wherein the animal is fed an **antibody** produced against **lipase**, an enzyme which is required for fat absorption. Avian egg-derived anti-**lipase antibodies** are disclosed for treating obesity in a mammal or an avian. Also, avian egg-derived **antibodies** (IgYs) against **gastrointestinal** enzyme such as amylase, trypsin, chymotrypsin, protease and other enzyme or antigen are used for reducing absorption of nutrients such as proteins, carbohydrates and lipids. These **antibodies** are mixed in **food** (concd., additive-added, refrigerated or frozen food) for human or animal consumption.

IT Fats and Glyceridic oils, biological studies

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(absorption; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Bird (Aves)
Chicken (Gallus domesticus)
Digestive system mucosa
Duck
Egg (animal)
Egg yolk
Encapsulation
Feed additives
Food
Freeze drying
Frozen foods
Goose
Liposomes (drug delivery systems)
Liquids
Mammal (Mammalia)
Mold (fungus)
Nutrients
Obesity
Oral drug delivery systems
Pheasant
Pigeon
Powders
Primate
Quail
Ruminant
Spray drying
Turkey
Yeast
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT **Antibodies**
IgY
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Carbohydrates, biological studies
Lipids, biological studies
Proteins (general), biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Antigens
Monoclonal **antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(fat-hydrolytic; avian egg-derived anti-**lipase** or anti-

gastrointestinal enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Concentration (process)
Refrigeration
(food; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Enzymes, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(gastrointestinal; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Animal cell line
Bacteria (Eubacteria)
Plant (Embryophyta)
(lipase; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT Mammal (Mammalia)
(monogastric; avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

IT 9000-92-4, Amylase 9001-62-1, Lipase 9001-92-7, Protease 9002-07-7, Trypsin 9004-07-3, Chymotrypsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(avian egg-derived anti-**lipase** or anti-**gastrointestinal** enzyme **antibodies** are prepd. for decreasing fat absorption or absorption of nutrients and for treating obesity)

L10 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:713196 CAPLUS
DOCUMENT NUMBER: 128:11377
TITLE: Immunological techniques for the characterization of digestive lipases
AUTHOR(S): Aoubala, Mustapha; Douchet, Isabelle; Bezzine, Sofiane; Hirn, Michel; Verger, Robert; De Caro, Alain
CORPORATE SOURCE: Laboratorie de Lipolyse Enzymatique, UPR 9025, IFRC1 du CNRS, Marseille, 13402, Fr.
SOURCE: Methods Enzymol. (1997), 286(Lipases, Part B), 126-149
CODEN: MENZAU; ISSN: 0076-6879
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe the prepn. and possible application of polyclonal and monoclonal **antibodies** to human **gastric lipase** and human pancreatic lipase obtained from gastric and pancreatic juices, resp.
AB The authors describe the prepn. and possible application of polyclonal and monoclonal **antibodies** to human **gastric lipase** and human pancreatic lipase obtained from gastric and pancreatic juices, resp.
ST **lipase** characterization **antibody**

L10 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:100030 CAPLUS
DOCUMENT NUMBER: 118:100030
TITLE: Epitope mapping and immunoinactivation of human gastric **lipase** using five monoclonal **antibodies**
AUTHOR(S): Aoubala, Mustapha; Daniel, Cecile; De Caro, Alain; Ivanova, Margarita G.; Hirn, Michel; Sarda, Louis; Verger, Robert
CORPORATE SOURCE: Lab. Lipolyse Enzym., Cent. Natl. Rech. Sci., Marseille, Fr.
SOURCE: Eur. J. Biochem. (1993), 211(1-2), 99-104
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five monoclonal **antibodies** (mAb) directed against human gastric **lipase** (HGL) were produced by hybridization of myeloma cells with spleen cells of BALB/c immunized mice. All these mAb belong to the IgG1 class with a .kappa. light chain. The effects of these mAb on the enzymic activity of HGL were studied and used to define 3 classes of antibodies, depending upon their immunoinactivation properties. As detd. by ELISA and immunoinactivation studies, 4 overlapping epitopes were found to be part of the functional sites of the enzyme. The mAb appear to be suitable probes for studying the lipid binding and catalytic domains of HGL. The results of the ELISA additivity test were used to describe tentatively the epitopes of HGL in terms of a schematic spatial map.

TI Epitope mapping and immunoinactivation of human gastric **lipase** using five monoclonal **antibodies**

AB Five monoclonal **antibodies** (mAb) directed against human gastric **lipase** (HGL) were produced by hybridization of myeloma cells with spleen cells of BALB/c immunized mice. All these mAb belong to the IgG1 class with a .kappa. light chain. The effects of these mAb on the enzymic activity of HGL were studied and used to define 3 classes of antibodies, depending upon their immunoinactivation properties. As detd. by ELISA and immunoinactivation studies, 4 overlapping epitopes were found to be part of the functional sites of the enzyme. The mAb appear to be suitable probes for studying the lipid binding and catalytic domains of HGL. The results of the ELISA additivity test were used to describe tentatively the epitopes of HGL in terms of a schematic spatial map.

ST gastric lipase epitope mapping; monoclonal **antibody** **gastric lipase**

IT Enzyme functional sites
(monoclonal **antibodies** to, of human **gastric lipase**)

IT **Immunoglobulins**
RL: BIOL (Biological study)
(G1, monoclonal, to **gastric lipase** of humans, epitope mapping for)

IT Enzyme functional sites
(substrate-binding, monoclonal **antibodies** to, of human **gastric lipase**)

IT 60514-49-0, 1,2-Didecanoyl-sn-glycerol
RL: RCT (Reactant)

(hydrolysis of, by human **gastric lipase**, monoclonal **antibodies** inhibition of)

L15 ANSWER 20 OF 35 USPATFULL
ACCESSION NUMBER: 1999:4416 USPATFULL
TITLE: Lipase from human gastric mucosal tissue
INVENTOR(S): Lowe, Peter Anthony, Reading, United Kingdom
PATENT ASSIGNEE(S): Celltech Limited, Berkshire, United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5858755		19990112
APPLICATION INFO.:	US 1996-735956		19961023 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-340123, filed on 15 Nov 1994, now patented, Pat. No. US 5691181 which is a division of Ser. No. US 1993-97619, filed on 27 Jul 1993, now abandoned which is a continuation of Ser. No. US 1992-996488, filed on 28 Dec 1992, now abandoned which is a continuation of Ser. No. US 1991-750704, filed on 20 Aug 1991, now abandoned which is a continuation of Ser. No. US 1990-554062, filed on 26 Jun 1990, now abandoned which is a continuation of Ser. No. US 1986-865564, filed on 21 Apr 1986, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1984-2120	19840821

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Hendricks, Keith D.
LEGAL REPRESENTATIVE: Spencer & Frank
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 953
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A human gastric lipase protein for use in the treatment of lipase deficiency. A process is described for producing gastric lipase using recombinant DNA technology to produce a host organism (for example E. coli) capable of producing a methionine-gastric lipase or precursor of the gastric lipase which may be cleaved to yield the gastric lipase. The host organism is transformed with a vector including a gene coding for a methionine-gastric lipase or a precursor of gastric lipase. The precursor protein is for example, pregastric lipase protein, or a fusion protein comprising gastric lipase and a heterologous protein. A pharmaceutical composition in unit dosage or liquid form is described.

SUMM The lipolysis of **dietary** fat is an important feature of the digestive systems of higher animals. The digestive process is made possible by enzyme. . .

SUMM . . . portion (MW about 2000) attached to an Asn residue at position 166 in the amino acid sequence. The total molecular **weight** of the enzyme is therefore approximately 52000. The catalytic activity of pancreatic lipase is complex since there exists a phase. . . for the enzyme to interact with the substrate a coenzyme known as colipase is necessary. Colipase is a low molecular **weight** protein which adsorbs to the solution/lipid interface and then acts as an anchor for

lipase, allowing interaction between the enzyme. . .

SUMM . . . levels of pancreatic lipase. At birth the high carbohydrate nutrition of the foetal period is replaced by a high fat **diet** as the infant begins to take its mothers milk. Fats account for about half an infant's calorie input. The pancreatic. . .

SUMM a. Molecular **weight** approximately 45,000,

SUMM We further provide a DNA sequence coding for at least the amino acid sequence of human gastric **lipase** or human pre gastric **lipase** as shown in FIG. 3 of the accompanying drawings. Preferably the DNA sequence is as shown in FIG. 3.

SUMM . . . host organism may be any organism which may be transformed by a vector including a gene coding for a gastric **lipase** protein such that expression of the gene occurs. Suitable such host organisms include bacteria (for example E.coli), yeasts (for example. . . culture. Preferably, where the host organism is a bacterium or a yeast the vector includes a gene coding for methionine-gastric **lipase** or a fusion protein, and when the host organism is a mammalian cell in tissue culture the vector preferably includes a gene coding for pregastric **lipase**.

SUMM In a tenth aspect of the invention we provide an **antibody** having specificity for an antigenic determinant of a **gastric lipase** protein. The **antibody** may be a polyclonal or a monoclonal **antibody** but is preferably a monoclonal **antibody**. The **antibody** may be labelled with a detectable marker, for example a radioactive isotope, for use in immunoassay.

SUMM In an eleventh aspect of the invention we provide a pharmaceutical composition comprising a gastric **lipase** protein and a pharmaceutically acceptable excipient. Preferably the **lipase** protein is a human gastric **lipase** produced by a process of the second or third aspect of the invention. The pharmaceutical composition is provided for use in the treatment of **lipase** deficiency. Preferably the composition is formulated for oral administration.

SUMM To product a unit dosage form the gastric **lipase**, in a suitable form, may be mixed with a solid pulverulent non-pharmaceutically active carrier such as lactose, saccharose, sorbitol, mannitol,. . . the coating to facilitate identification of the unit dosage form. Soft or hard capsules may be used to encapsulate gastric **lipase** as a liquid or solid preparation.

DRWD . . . of human gastric lipase (Lane A--purified human gastric lipase, Lane B--partially purified extract of human gastric lipase, Lane C--standard molecular **weight** markers),

DETD . . . of Tiruppathi et al (1982) Biochim. Biophys. Acta. 712 692-697. This procedure produced pure human gastric lipase with a molecular **weight** of approximately 50,000 as judged by SDS PAGE. (Lammeli (1970) Nature 277 68-685), FIG. 1 shows a polyacrylamide SDS gel. . . Lane B, a partially purified extract of human gastric aspirate (approximately 10 .mu.g), Lane C, a series of standard molecular **weight** markers. The enzyme had an activity of approximately 600 lipase units per mg (unit-micromoles of free fatty acid formed per. . .

DETD Characterisation of Authentic Human Gastric Lipase Determination of Molecular **Weight**

DETD . . . purified to homogeneity and subjected to electrophoresis in SDS polyacrylamide gels migrated as a single band with an apparent molecular **weight** of approximately 50,000 (FIG. 1). Gel filtration of impure human gastric lipase on Sephadex G150 resulted in a calculated molecular **weight** in approximate agreement with that obtained by polyacrylamide gel electrophoresis. A molecular **weight** of 45,000 has been estimated by Tiruppathi et al (1982), see above, using gel filtration on Sephadex G100. It is therefore concluded that the

purified human gastric lipase is active as a monomer of approximately 50,000 molecular **weight**.

DETD . . . Blue staining. Digestion of human gastric lipase with Endoglycosidase H resulted in the generation of a series of lower molecular **weight** forms with a minimum molecular **weight** of approximately 41,000. Endoglycosidase H digestion results in the removal of N linked carbohydrate moieties from glycoproteins containing these residues. This cleavage produces an apparent lowering of the molecular **weight** of the deglycosylated protein. This lowering of molecular **weight** maybe visualised by increased mobility of the deglycosylated protein on SDS PAGE. That Endoglycosidase treatment of human gastric lipase results in an apparent decrease of molecular **weight** from approximately 50,000 to approximately 41,000 indicates that approximately 20% of the enzyme (by **weight**) is composed of carbohydrate.

DETD . . . P. S. (1980) PNAS USA, 77 5201-5205). By this technique polyadenylated stomach RNA was separated on the basis of molecular **weight** by gel electrophoresis and probed with a cDNA clone of the rat lingual lipase gene labelled by nick translation (Rigby. . .

DETD . . . from the DNA sequence indicates that mature human gastric lipase consists of a 379 amino acid protein. The predicted molecular **weight** of this mature protein is 43,162 which is in close agreement with the molecular **weight** determined for the deglycosylated enzyme by SDS PAGE. The total amino acid composition of the mature enzyme produced from the. . . fixation of pancreatic lipase to lipid (Guidoni, A. et al 1981, Biochim. Biophys. Acta. 660, 148-150) and reacts with micellar **diethyl**-p-nitrophenyl phosphate (Rouard, M. et al 1978, Biochim. Biophys. Acta. 530, 227-235).

It is present in the sequence: 152 Gly- His-. . .

DETD . . . Lane D. This analysis indicated that E103(S)/pMG197 expressed human gastric lipase as a prominent protein migrating with an apparent molecular **weight** of approximately 38,000. The discrepancy between the apparent molecular **weights** of natural human gastric lipase (approx. 50,000) and recombinant human gastric lipase (approx. 38,000) could be due to the inability of E.coli to carry out glycosylation. Unglycosylated human gastric lipase has a molecular **weight** of 43,162 as predicted by amino acid sequence derived from the DNA sequence of the cloned gene.

DETD . . . extract and the cell debris fraction. A prominent band of human gastric lipase is seen migrating with an apparent molecular **weight** of approximately 40,000 in the total extract and insoluble debris fraction. Virtually no human gastric lipase was detectable in the. . . analysis was repeated on yeast MD40/4C containing pYC3 with similar results. Again, a discrepancy is seen between the apparent molecular **weights** of natural human gastric lipase (approx. 50,000) and recombinant human gastric lipase (approx. 40,000). This may be due to an. . .

L15 ANSWER 24 OF 35 USPATFULL

ACCESSION NUMBER: 1998:44880 USPATFULL
TITLE: Immunoglobulin and fiber-containing composition for human gastrointestinal health
INVENTOR(S): Paul, Stephen M., San Clemente, CA, United States
PATENT ASSIGNEE(S): Metagenics, Inc., San Clemente, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5744134		19980428
APPLICATION INFO.:	US 1996-674115		19960701 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-437316, filed on 9 May 1995, now patented, Pat. No. US 5531989 which is a continuation-in-part of Ser. No. US 1994-331140, filed on 28 Oct 1994, now patented, Pat. No. US 5531988
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Nutter, Nathan M.
LEGAL REPRESENTATIVE: Thorpe, North & Western
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A composition for restoring and maintaining gastrointestinal health comprises 40-60% by **weight** of an immunoglobulin composition comprising concentrated immunologically active immunoglobulins and 40-60% by **weight** of soluble **dietary** fiber selected from inulin, fructo-oligosaccharides, pectin, guar gum, and mixtures thereof. The immunoglobulin and fiber-containing composition can optionally contain one or more of a beneficial human intestinal microorganism, components of a non-immune natural defense system, an iron-sequestering molecule, and gluconic acid. Preferred beneficial human intestinal microorganisms include lactobacilli and bifidobacteria.

The immunologically active immunoglobulins are preferably purified from bovine milk, milk products, or whey. Methods of use are also described.

AB A composition for restoring and maintaining gastrointestinal health comprises 40-60% by **weight** of an immunoglobulin composition comprising concentrated immunologically active immunoglobulins and 40-60% by **weight** of soluble **dietary** fiber selected from inulin, fructo-oligosaccharides, pectin, guar gum, and mixtures thereof. The immunoglobulin and fiber-containing composition can optionally contain one. . .

SUMM . . . binding and inactivating foreign antigens such as pathogenic bacteria, viruses, fungi, and protozoa that are detrimental to gastrointestinal health; soluble **dietary** fiber that provides the advantages typically offered by **dietary** fibers with the additional advantages of not affecting blood glucose or insulin levels, being readily fermented by the intestinal microflora. . .

SUMM . . . or immunoglobulins capable of providing passive immunity against various pathogens and their toxic by-products. Antibodies or immunoglobulins are high molecular **weight** proteins produced in the bodies of mature animals that enhance immunity to infection by bacteria, viruses, fungi, protozoa, and the. . .

SUMM . . . infection have been prevented by treatment with an

immunoglobulin concentrate from bovine milk. C. Tacket et al., Protection by Milk **Immunoglobulin** Concentrate against **Oral** Challenge with Enterotoxigenic Escherichia Coli, 318 N. Engl. J. Med. 1240 (1988).

SUMM Soluble fiber in the **diet** is well known for its salutary effects on gastrointestinal health. Such effects include providing bulk to the stool, decreasing the pH of the gastrointestinal tract, producing volatile fatty acids, decreasing intestinal transit time, and beneficially influencing various blood parameters. **Dietary** fiber has also been shown to have a beneficial effect on cholesterol and lipid metabolism that results in decreased serum. . . phospholipids and an improved (increased) HDL to LDL ratio. A study on laboratory animals showed that adding fiber to the **diet** decreases the incidence of bacterial translocation, i.e. crossing the intestinal barrier and entering systemic circulation. C. Palacio et al., **Dietary** Fiber: Physiologic Effects and Potential Applications to Enteral Nutrition, in Clinical Nutrition: Enteral and Tube Feeding (2d. ed., 1990). Nutritional and epidemiological studies have indicated that a general increase in the consumption of **dietary** fiber may play a role in preventing deleterious effects of oxygen free radicals that have been accused of being involved. . .

SUMM While prior art formulas as **dietary** supplements containing soluble **dietary** fiber or immunoglobulins are known and are generally suitable for their limited purposes, they possess certain inherent deficiencies that detract from their overall utility in restoring and maintaining gastrointestinal health. For example, a **dietary** supplement containing soluble **dietary** fiber without concentrated immunoglobulins lacks means for binding and inactivating foreign antigens such as pathogenic bacteria, viruses, fungi, and protozoa that can infect the gastrointestinal tract and are detrimental to the health thereof. Similarly, a **dietary** supplement containing concentrated immunoglobulins without soluble **dietary** fiber lacks means for providing bulk to the stool, decreasing the pH of the gastrointestinal tract, producing volatile fatty acids,. . . growth of pathogenic bacteria, reducing levels of toxic amines, and lowering the pH of the gastrointestinal tract. Further, prior art **dietary** supplements fail to provide components, such as lactoperoxidase and thiocyanate, that strengthen the body's natural non-immune defense system or LP-system.. . .

SUMM In view of the foregoing, it will be appreciated that a composition for improving and maintaining **gastrointestinal** health comprising an **immunoglobulin** preparation containing immunoglobulins that bind and inactivate pathogenic microorganisms in the gastrointestinal tract and soluble **dietary** fiber that provides the typical advantages of **dietary** fiber and additionally is low in calories, does not affect blood glucose or insulin levels, and favors the growth of. . .

SUMM It is an object of the present invention to provide a composition for use as a **dietary** supplement that benefits human gastrointestinal health when administered orally.

SUMM It is also an object of the invention to provide a composition for use as a **dietary** supplement that, when ingested, is effective for treating ailments due to gastrointestinal pathogens such as bacteria, viruses, fungi, or protozoa.

SUMM It is another object of the invention to provide a composition for use as a **dietary** supplement that, when ingested, results in decreased serum cholesterol, triglycerides, and phospholipids and an increased HDL to LDL ratio.

SUMM It is still another object of the invention to provide a composition for use as a **dietary** supplement that aids in preventing deleterious effects of oxygen free radicals.

SUMM It is yet another object of the invention to provide a composition for

use as a **dietary** supplement that bolsters the body's immune system and the natural non-immune system, the LP system.

SUMM It is a further object of the invention to provide a composition for use as a **dietary** supplement that inhibits detrimental iron-catalyzed processes in the body.

SUMM It is a still further object of the invention to provide a method of use for a **dietary** supplement composition that benefits human gastrointestinal health when administered orally.

SUMM These and other objects may be accomplished by providing an immunoglobulin and fiber-containing composition for use as a **dietary** supplement for restoring and maintaining gastrointestinal health comprising in percent by **weight**

SUMM (b) about 40 to about 60% of soluble **dietary** fiber, wherein said fiber is a member selected from the group consisting of inulin, fructo-oligosaccharides, pectin, guar gum, and mixtures thereof. The immunoglobulin and fiber-containing composition can optionally contain about 0 to about 20% by **weight** of a beneficial human intestinal microorganism selected from the group consisting of lactobacilli and bifidobacteria. Preferably, the beneficial human intestinal microorganism is present in an amount in the range of about 0.1 to about 20% by **weight**, and more preferably of about 5 to about 10% by **weight**. The immunoglobulin and fiber-containing composition can also optionally contain one or more of the following ingredients:

SUMM

	Ranges in Percent by **Weight**	
Ingredient	Broad	Preferred
Lactoperoxidase	0-0.0300%	0.0001-0.0300%
Thiocyanate salt	0-0.0500%	0.0001-0.0500%
Lactoferrin	0-0.1000%	0.0001-0.1000%
Gluconic acid	0-10%	0.4-10%

SUMM . . . of orally administering an effective amount of an immunoglobulin and fiber-containing composition for promoting gastrointestinal health comprising in percent by **weight**

SUMM (b) about 40 to about 60% of soluble **dietary** fiber, wherein the fiber is a member selected from the group consisting of inulin, fructo-oligosaccharides, pectin, guar gum, and mixtures. . .

DETD . . . composition is sold under the trademark "PROBIOPLEX" by Metagenics, Inc. (San Clemente, Calif.) PROBIOPLEX contains (1) about 55-60 parts by **weight** of an immunoglobulin concentrate from bovine whey wherein at least about 7% by **weight** of the total solids in the concentrate is immunologically active immunoglobulins, (2) about 35-40 parts by **weight** of a mixture of carbohydrates including rice maltodextrin and lactose, and (3) about 5-10 parts by **weight** of lipid including lecithin. Thus, at least about 3.6% by **weight** of the total PROBIOPLEX composition comprises immunologically active immunoglobulins. The carbohydrates and lipids function as inert carriers for the immunoglobulins.. . .

DETD The advantages of soluble **dietary** fiber have been briefly reviewed above. Inulin is one such fiber that is composed of a mixture of oligomers and. . . in many plants including onion, asparagus, artichoke, and many cereals. Chicory root and Jerusalem artichoke each contain about 70% by **weight** of inulin. Inulin has been an important food in Europe for many years and is currently being used as a source of **dietary** fiber, for replacing fat in the **diet**, and for promoting growth of beneficial bacteria in the intestine. In the U.S., inulin is added to all types of. . .

DETD Fructo-oligosaccharides (FOS) are another type of soluble

dietary fiber. FOS is widely distributed in nature and is found in honey, beer, onion, asparagus, Chinese chive, banana, maple sugar,. . .

DETD . . . lactic acids. As a consequence of this fermentation, a considerable amount of bacterial mass is produced, which increases stool wet **weight**. The short chain fatty acids are absorbed by the large intestine and are further metabolized in the liver. This allows. . . of energy conversion is markedly lower than with other carbohydrates. This phenomenon underlies the low calorie content of fructans and **dietary** fibers.

DETD . . . Fructooligosaccharides on Intestinal Flora and Human Health, 5 Bifidobacteria Microflora 37-50 (1986). When inulin and FOS are administered in the **diet**, the bifidobacteria increase significantly, becoming the predominant bacteria in the intestinal population, and the clostridia, which are a measure of. . .

DETD . . . Neosugar on the Lipid Metabolism of Experimental Animals, Proc. 1st Neosugar Res. Conference, Tokyo (1982), that fructo-oligosaccharides (FOS) in the **diet** of experimental animals cause reduction of blood sugar, serum cholesterol, triglycerides, and phospholipids; significant improvement in the HDL/LDL ratio; an. . .

DETD . . . the following positive effects are obtained by addition of inulin and/or fructo-oligosaccharides (FOS) to a composition for use as a **dietary** supplement according to the present invention: reduction of intestinal disorders, enhancement of a balanced intestinal microflora, and remediation of constipation.

DETD Other preferred **dietary** fibers according to the present invention include pectin and guar gum. Pectin is a highly water soluble, noncellulosic polysaccharide fiber. . . the primary cell walls of plants. Rich sources of pectin include lemon and orange rinds, which contain about 30% by **weight** of this polysaccharide. Pectin occurs naturally as a partial methyl ester of .alpha.-(1.fwdarw.4) linked D-polygalacturonate sequences interrupted with (1.fwdarw.2)-L-rhamnose residues.. . .

DETD . . . and guar gum have several beneficial effects on the gastrointestinal tract, such as maintaining the morphology of intestinal villi, increasing **lipase** activity in the small bowel, delaying gastric emptying time, increasing intestinal transit time, and promoting increased fecal production of short chain fatty acids. It is believed that pectin and guar gum in the **diet** lower blood glucose and serum cholesterol levels, B. Flourie et al., The Effect of Pectin on Jejunal Glucose Absorption and Unstirred Layer Thickness in Normal Man, 25 Gut 1936 (1984). Also, **dietary** fiber supplementation with pectin or guar gum has also been found to significantly suppress the incidence of colon cancer. G.. . . the fruit reduces the insulin response to the sugar in the fruit and prevents "rebound" hypoglycemia. D. Jenkins et al., **Dietary** Fiber, Fiber Analogues and Glucose Tolerance, Importance of Viscosity, 1 Br. Med. J. 1392 (1978). Further, pectin and guar gum. . .

DETD . . . include ingested food, catalase-negative bacteria, and cigarette smoke and other pollutants. The production of reactive free radicals during metabolism of **dietary** fat can explain some the biological damage such as loss of membrane function, inactivation of membrane-bound enzymes, and inactivation of essential molecules located inside the cell. Other tests have shown that a large amount of fat in the **diet** can be a presumptive carcinogen. H. Hidaka et al., Effects of Fructooligosaccharides on Intestinal Flora and Human Health, 5 Bifidobacteria. . .

DETD As reviewed above, **immunoglobulin** concentrates from milk contain immunologically active **immunoglobulins** that are capable of binding pathogenic microorganisms such as bacteria, viruses,

fungi, and protozoa. Such **immunoglobulin** concentrates can be prepared from any starting material containing sufficient concentrations of immunologically active **immunoglobulins**, such as milk, whey, blood, and the like. An economically viable source of such **immunoglobulins** is the whey byproduct of the cheese making process. It has been estimated that approximately 85 million metric tons of. . . economically utilized, and thus are discarded. The whey byproduct of cheese making, therefore, presents an inexpensive and ready source of **immunoglobulins**.

DETD . . . Although these techniques are useful for producing food products, they almost universally destroy or substantially reduce the immunological activity of **immunoglobulins** in the concentrate by exposing the raw milk, whey, or protein concentrate to (1) excessive thermal (time and temperature) conditions,. . .

DETD . . . and Lactobacillus Feeding on Human Intestinal Bacterial Enzyme Activity, 39 Amer. J. Clin. Nutr. 756 (1984). These results suggest that **dietary** supplementation with L. acidophilus may reduce the risk of developing colon cancer.

DETD . . . of the bacterial population. Upon weaning or upon the occurrence of perturbations such an infection, vaccination, a sudden change in **diet**, and even the weather can upset the balance of microorganisms in the gastrointestinal tract of these babies. Bifidobacteria can also. . . due to a reduction of secreted gastric juices. The bifidobacterial population in adults is much more stable, however changes in **diet**, administration of antibiotics, exposure to gamma radiation or X-rays, disease, stress, and other disturbances can result in overgrowth of potentially. . . of carcinogenic metabolites. Reestablishment of a normal balance of gastrointestinal flora can be accelerated, and such normal balance maintained, with **dietary** administration of lactobacilli and/or